A cross-sectional study of patients with prosthetic mitral valves at a tertiary centre in Johannesburg, South Africa

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Background. There is a high incidence of rheumatic valvular heart disease involving the mitral valve in Soweto, Johannesburg. Many of these patients go on to have mitral valve replacement (MVR). Data regarding clinical and echocardiographic characteristics of patients with prosthetic mitral valves are scarce in South Africa.

Objective. To document the clinical and echocardiographic profiles of contemporary patients with MVR.

Methods. Clinical, electrocardiographic and echocardiographic data in these patients were collected prospectively from March 2020 to August 2021 at Chris Hani Baragwanath Academic Hospital prosthetic valve clinic.

Results. The study included 186 participants with a median (interquartile range (IQR)) age of 52 (41 - 60) years. Of these, 96% were of black African ethnicity (79% female). The median (IQR) body mass index (BMI) among participants was 27 (23.5 - 30.4) kg/m^2, with 29% of participants classified as obese (BMI >30 kg/m^2). Eighty-two percent of patients had New York Heart Association class 1 dyspnoea. The most common complications were atrial fibrillation (AF, 39%), heart failure (HF, 25%) and stroke (13%). There were two cases of previously documented prosthetic valve thrombosis, two cases of prosthetic valve endocarditis, two of paravalvular regurgitation and one with structural valve deterioration. Seventy percent of patients had subtherapeutic international normalised ratios (INRs), with a median (IQR) INR of 2.55 (2.03 - 2.92). Forty-seven percent of patients had a left ventricular ejection fraction (EF) of <40%. Seventy-four percent of participants were on some combination of guideline-directed medical therapy for HF with reduced EF, although only 12% were on at least three medications. Pulmonary hypertension was present in 37% of patients, with a median (IQR) pulmonary artery systolic pressure of 28.5 (17 - 41) mmHg. Tricuspid annuloplasty ring was noted in a minority (12 patients).

Conclusion. The contemporary patients with MVR were middle-aged obese females with significant AF burden, residual left ventricular dysfunction that was suboptimally managed, and subtherapeutic INR.

Keywords: cardiology, valvular heart disease, prosthetic heart valves, heart failure

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In the peri-urban setting of Soweto, Johannesburg, South Africa (SA),valvular heart disease is prevalent.[1] Rheumatic heart disease (RHD) is a common aetiology in this setting, with a recent estimated incidence of 23.5 cases per 100 000 population per year.[1] Previous studies show that ~36% of all newly diagnosed valvular lesions are due to RHD, with 89% of cases involving the mitral valve.[1] Additionally, patients with mitral valve disease in this setting tend to be older and have morphological characteristics that favour replacement over repair.[2] There is also an increasing incidence of infective endocarditis among younger patients in urban settings in SA, and up to 50% of these cases require surgical intervention.[2-5] In addition, with an ongoing epidemiological transition towards more diseases of lifestyle and elderly age, it can be expected that there will be more cases of degenerative valvular disease.[6]

Despite recent improvements in technology, medical therapy and surgical techniques, many patients still have ongoing medical issues after valve replacement surgery (an entity termed 'prosthetic valve disease').[7,8] The complications of prosthetic valve disease include paravalvular regurgitation, structural valvular deterioration, pannus formation, endocarditis, thrombosis and embolism, anticoagulation-related haemorrhage and haemolysis. Thus these are complex patients who require adequate monitoring and appropriate therapy. In this way, complications can be prevented, detected early and managed timeously.[7]

Developed nations have large databases describing their prosthetic valve populations – the primary aetiology being degenerative.[8,9] In comparison, there are minimal data in the SA setting. We therefore sought to systematically document the clinical and echocardiographic outcomes of these patients in our setting.

Objectives

To document the clinical and echocardiographic profiles and to evaluate the types of morbidity of patients with prosthetic mitral valve replacement (MVR).

Methods

This was a cross-sectional descriptive study of patients with prosthetic mitral valves at Chris Hani Baragwanath Academic Hospital. It was conducted from March 2020 to August 2021 (while the initial study period was planned from March 2020 to August 2020, the coronavirus pandemic delayed data collection). The investigator collected demographic, clinical and electrocardiographic data, while the cardiac technologist collected echocardiographic data (all part of the routine care of patients). This was done once-off and with the informed consent of the participants.

Each patient had their vital signs (including blood pressure, pulse rate, respiratory rate and temperature), weight and height recorded. This was

followed by a clinical interview by the primary investigator, specifically inquiring about the history of their valve replacement, indications, complications, functional status and associated comorbidities. Finally, this information was supplemented with data from their available clinical records (including their international normalised ratio (INR) clinic records).

Transthoracic echocardiography was then performed on all patients in the study using the Philips EPIQ 7C iE33 (Philips, the Netherlands), and images were obtained according to standard protocol. Measurements were done according to the American Society of Echocardiography chamber quantification guidelines of 2015,[10] as well as the European Society of Cardiology and American Heart Association guidelines for managing patients with valvular heart disease,[11,12] and were indexed to body surface area. In all cases, assistance from an experienced cardiologist was sought.

The biochemical profiles of patients were obtained from recent routine measurements (such as full blood counts, urea, creatinine, electrolytes, lactate dehydrogenase and international normalised ratios (INRs)).

We recruited 186 patients to obtain a statistically significant result. Inclusion criteria were age >18 years and patients with prosthetic MVR (with or without other prosthetic valves). Exclusion criteria were refusal to participate and isolated non-mitral valve replacement.

Ethical approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (ref. no. M200905). The study was performed per the World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects.

Statistical analysis

The data analysis was done using descriptive statistics, where categorical data were expressed as percentages, and continuous variables were expressed as either mean or median (standard deviation (SD)) or interquartile range (IQR). Continuous variables were compared using Student's *t*-test, and data with non-parametric distribution were assessed by Fisher's exact test. A *p*-value <0.05 was considered statistically significant. Pearson's correlation was used to correlate variables.

Poisson regression with robust error variance was used to determine the strength and direction of association between demographic, clinical, electrocardiographic and echocardiographic findings of patients who had MVR with the left ventricular ejection fraction (LVEF) <40%. Variables that had *p*-values <0.2 in univariable analysis were eligible for inclusion in an initial multivariable model, but were eliminated in a stepwise backwards approach until eight variables remained in the model. Prevalence rate ratios associated with the variables were reported with 95% confidence intervals (CIs).

Results

Ninety-six percent of participants were of black African descent (Table 1). The study population had a median (IQR) age of 52 (40 - 61) years, and was predominantly of female biological sex (79%). Most patients were overweight, with a median body mass index (BMI) of 26.6 kg/m^2, while 29% were obese, with a BMI >30 kg/m^2. The most common comorbidities noted were hypertension (36%) and diabetes

Table 1. Demographic and clinical characteristics of patients with mitral valve replacement and statistical comparison

Characteristic	All, *N*=186	Female, *n*=147	Male, *n*=39	*p*-value	MV+, *n*=64
Age, years, median (IQR)	52 (41 - 60)	53 (41 - 61)	47 (40 - 58)	0.153	52 (41 - 60)
Sex, *n* (%)					
Female	147 (79.0)	-	-	-	44 (68.8)
Male	39 (20.9)	-	-	-	20 (31.2)
Race, *n* (%)					
Black African	178 (95.7)	141 (95.9)	37 (94.9)	0.662*	60 (93.8)
Coloured	4 (2.2)	3 (2.0)	1 (2.6)		2 (3.1)
Indian	2 (1.1)	1 (0.7)	1 (2.6)		1 (1.7)
White	2 (1.1)	2 (1.4)	0 (0.0)		1 (1.7)
BMI, kg/m^2, median (IQR)	26.6 (23.5 - 30.4)	27.7 (23.9 - 31.6)	23.6 (20.4 - 27.1)	<0.001	24.4 (23.0 - 28.4)
BMI >30, kg/m^2, *n* (%)	53 (28.5)	51 (34.7)	2 (5.1)	<0.001*	12 (18.8)
Body surface area, m^2, median (IQR)	2.62 (2.49 - 2.82)	2.59 (2.43 - 2.72)	2.99 (2.82 - 3.17)	<0.001	2.64 (2.46 - 2.86)
Comorbidity, *n* (%)					
Hypertension	67 (36)	60 (40.8)	7 (18.0)	0.009	19 (29.7)
Diabetes mellitus	15 (8)	15 (10.2)	0 (0.0)	0.037*	4 (6.3)
Dyslipidaemia	12 (7)	11 (7.5)	1 (2.6)	0.465*	3 (4.7)
HIV	20 (10.8)	13 (8.8)	7 (18.0)	0.103	4 (6.3)
Thyroidal illness	5 (3)	5 (3.4)	0 (0.0)	0.586*	2 (2.1)
Systolic BP, mmHg, median (IQR)	126 (115 - 143)	126 (116 - 144)	128 (113 - 140)	0.695	131 (119 - 146)
Diastolic BP, mmHg, median (IQR)	78 (70 - 85)	78 (71 - 86)	78 (69 - 85)	0.472	79 (71 - 86)
Pulse rate, bpm, median (IQR)	75 (65 - 82)	75 (65 - 83)	72 (63 - 78)	0.345	73 (65 - 81)
Operated valves, *n* (%)					
MV only	122 (65.6)	103 (70.1)	19 (48.7)	0.012	-
MV+	64 (34.4)	44 (29.9)	20 (51.3)		
NYHA functional class, *n* (%)					
I	152 (81.7)	115 (78.2)	37 (94.9)	0.056*	51 (79.7)
II	32 (17.2)	30 (20.4)	2 (5.1)		12 (18.8)
III	2 (1.1)	2 (1.4)	0 (0.0)		1 (1.6)
IV	0 (0)	0 (0.0)	0 (0.0)		0 (0.0)

MV+ = mitral valve plus others; IQR = interquartile range; EF = ejection fraction; BMI = body mass index; BP = blood pressure; bpm = beats per minute; MV = mitral valve; NYHA = New York Heart Association.
*Fisher's exact *p*-value.

mellitus (8%). Most patients were normotensive, not tachycardic and not in overt heart failure (HF) during assessment. Approximately two-thirds of patients had only had surgical intervention and replacement of the mitral valve (66%); the remaining patients had mitral valve and a combination of aortic and/or tricuspid valve surgery. In terms of functional status, 82% of patients were classified as New York Heart Association (NYHA) class I dyspnoea. The rest (17.2%) were classified as NYHA class II dyspnoea. As shown in Fig. 1, most patients in this study were operated on after the year 2000.

Thirty-nine percent of patients were in persistent/permanent atrial fibrillation (AF). HF admissions had occurred in 25% of all patients, and cerebrovascular accidents (CVAs) occurred in 13% of all patients. However, the aetiology of these (embolic v. haemorrhagic or other) was not reliably documented. There were two cases each of previously documented prosthetic valve endocarditis, thrombosis and paravalvular regurgitation, and only one of structural valve deterioration. This is further illustrated in Fig. 2.

Fig. 3 shows the number of patients on guideline-directed medical therapy for HF, with 74% on some combination of treatments.

Biochemical analysis (Table 2) revealed that 65% of patients had normal haemoglobin values at the last measurement, although only 109 in total had this measurement available. Of note, 17% of patients had anaemia of moderate to severe classification, as per World Health Organization definitions.[13] Renal function was normal in almost all patients (*n*=110; 86%) with these measurements available. Regarding anticoagulation, the INRs for patients on long-term warfarin therapy were striking, with 70% of patients having <70% of their measurements in a suitable therapeutic range, i.e. between 2.5 and 3.5. The median (IQR) INR among all participants was 2.55 (2.03 - 2.92). Approximately 10% of participants were HIV positive, and all these patients were on antiretroviral therapy (ART), with 14 of them virally suppressed. Three HIV-positive patients did not have any accessible record of recent CD4 counts or viral load.

Echocardiographic features

Approximately 50% of patients in this study had left ventricular systolic dysfunction, defined as an ejection fraction (EF) <40%[14] (Table 3). Most patients had evidence of possible elevated left ventricular filling pressures, as evidenced by a median (IQR) lateral E/e' (ratio of early diastolic filling to mitral annular velocity) of 17.4 (13.6 - 21.7) and a median (IQR) medial E/e' of 22.6 (16.4 - 28.8). Interestingly, only 18% of participants reported a NYHA functional class of II or higher. This could be due to the subjective nature of symptom reporting and the presence of mitral valve prostheses, which may offset mitral annular tissue Doppler measurements. Most patients (71%) had significant left atrial enlargement, with a median indexed left atrial volume of 44.4 mL/m^2. The median right ventricular (RV) basal diameter was 42 mm, while the median RV S' (RV systolic wave velocity) was 8.7 cm/s, indicating that most patients had enlarged and dysfunctional right ventricles. Pulmonary hypertension was present in 36.6% of patients, with a median (IQR) pulmonary artery systolic pressure of 28.5 (17 - 41) mmHg. A tricuspid annuloplasty ring was evident in 12 patients. Ninety-five

MV only, *n*=122	*p*-value	EF ≥40, *n*=99	EF <40, *n*=87	*p*-value	Year <2000, *n*=46	Year ≥2000, *n*=140	*p*-value
52 (40 - 60)	0.871	50 (38 - 61)	53 (43 - 60)	0.344	54 (45 - 63)	51 (40 - 60)	0.051
103 (84.4)	0.013	74 (74.8)	73 (83.9)	0.126	41 (89.1)	106 (75.7)	0.052
19 (15.6)		25 (25.2)	14 (16.1)		5 (10.9)	34 (24.3)	
118 (96.7)	0.825*	95 (95.7)	83 (95.4)	0.514*	45 (97.8)	133 (95.0)	0.999*
2 (1.6)		3 (3.0)	1 (1.2)		1 (2.2)	3 (2.1)	
1 (0.8)		1 (1.0)	1 (1.2)		0 (0.0)	2 (1.4)	
1 (0.8)		0 (0.0)	2 (2.3)		0 (0.0)	2 (1.4)	
27.1 (24.0 - 30.9)	0.018	25.5 (23.1 - 30.0)	27.1 (24.0 - 31.2)	0.271	29.2 (24.9 - 32.3)	25.7 (23.0 - 29.9)	0.003
41 (33.6)	0.033	25 (25.3)	28 (32.2)	0.296	20 (43.5)	33 (23.6)	0.009
2.62 (2.50 - 2.82)	0.939	2.62 (2.50 - 2.76)	2.62 (2.46 - 2.89)	0.761	2.59 (2.50 - 2.76)	2.64 (2.48 - 2.89)	0.408
48 (39.3)	0.192	34 (34.3)	33 (37.9)	0.648	21 (45.7)	46 (32.9)	0.117
11 (9.0)	0.510*	6 (6.1)	9 (10.3)	0.284	6 (13.0)	9 (6.4)	0.153
9 (7.4)	0.549*	3 (3.0)	9 (10.3)	0.069*	2 (4.4)	10 (7.1)	0.733*
16 (13.1)	0.213*	10 (10.1)	10 (11.5)	0.760*	1 (2.2)	19 (13.6)	0.029*
3 (2.5)	0.999*	4 (4.0)	1 (1.2)	0.373*	0 (0.0)	5 (3.6)	0.335*
124 (112 - 140)	0.092	125 (114 - 144)	128 (116 - 143)	0.834	131 (118 - 144)	125 (115 - 143)	0.257
78 (70 - 85)	0.565	76 (69 - 85)	79 (72 - 86)	0.108	78 (71 - 86)	78 (70 - 85)	0.640
76 (64 - 83)	0.278	75 (64 - 80)	75 (65 - 85)	0.168	75 (64 - 81)	75 (65 - 83)	0.551
-	-	64 (64.6)	58 (66.7)	0.772	34 (73.9)	88 (62.9)	0.171
		35 (35.4)	29 (33.3)		12 (26.1)	52 (37.1)	
101 (82.8)	0.819*	84 (84.8)	68 (78.2)	0.227*	36 (78.3)	116 (82.9)	0.452*
20 (16.4)		15 (15.2)	17 (19.5)		9 (19.6)	23 (16.4)	
1 (0.8)		0 (0.0)	2 (2.3)		1 (2.2)	1 (0.7)	
0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	

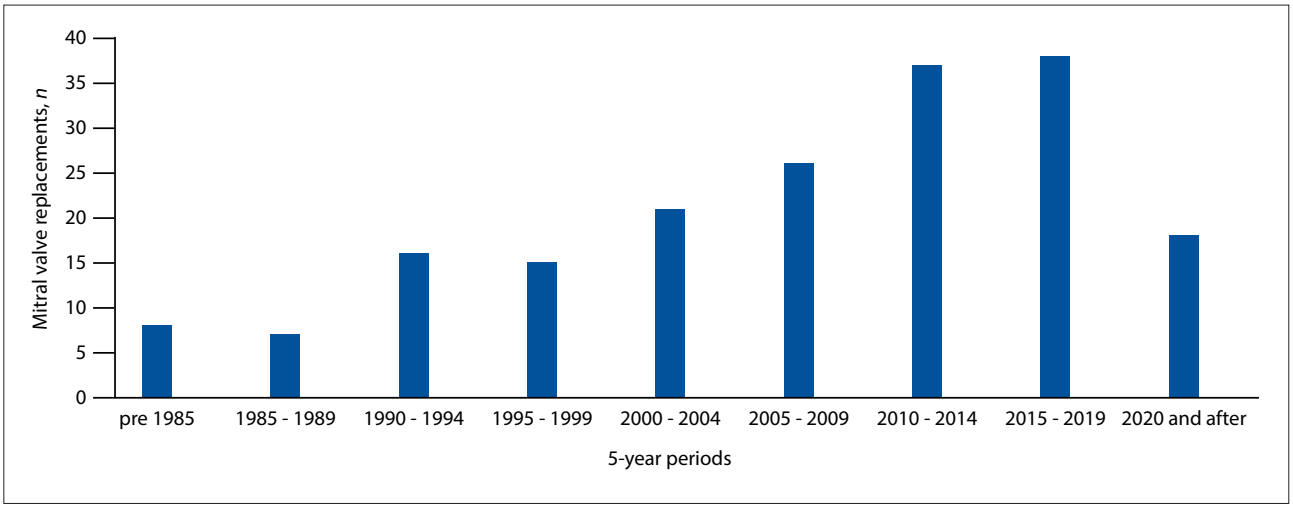

Fig. 1. Number of mitral valve replacements over time.

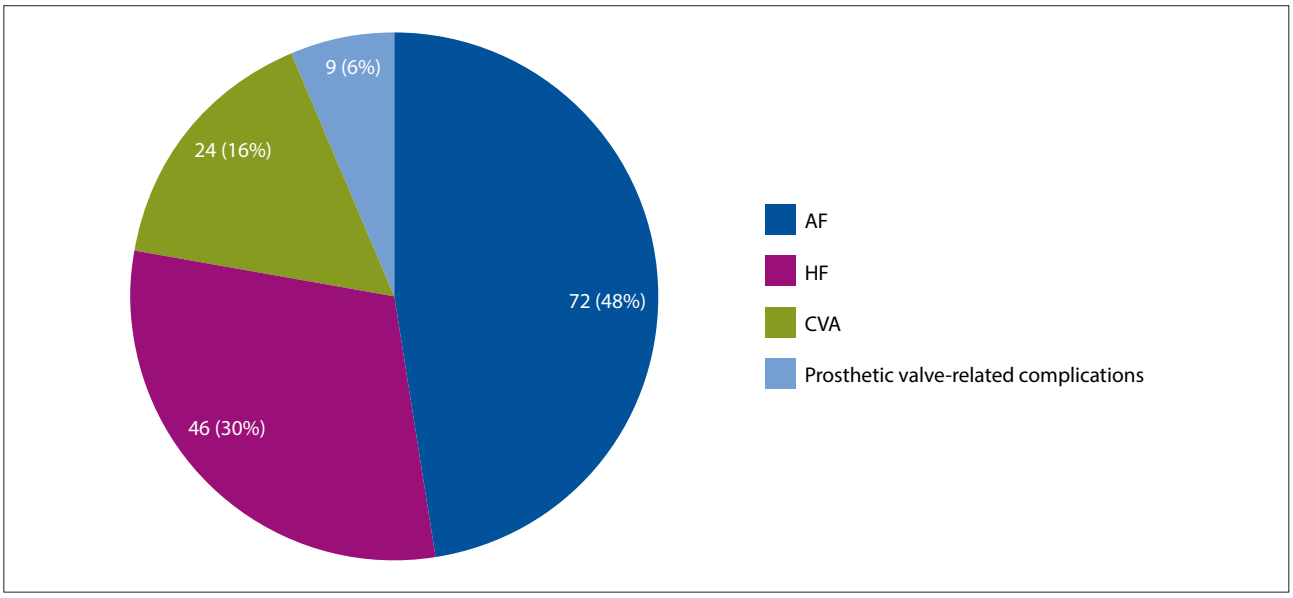

Fig. 2. Complications in patients with mitral valve replacement. Prosthetic valve-related complications: previously documented thrombosis (n=2), previously documented endocarditis (n=2), re-do surgery with no documented indication (n=2), paravalvular leak (n=2), previously documented structural valve deterioration (n=1). Patients may have had multiple complications. (AF = atrial fibrillation; HF = heart failure; CVA = cerebrovascular accident.)

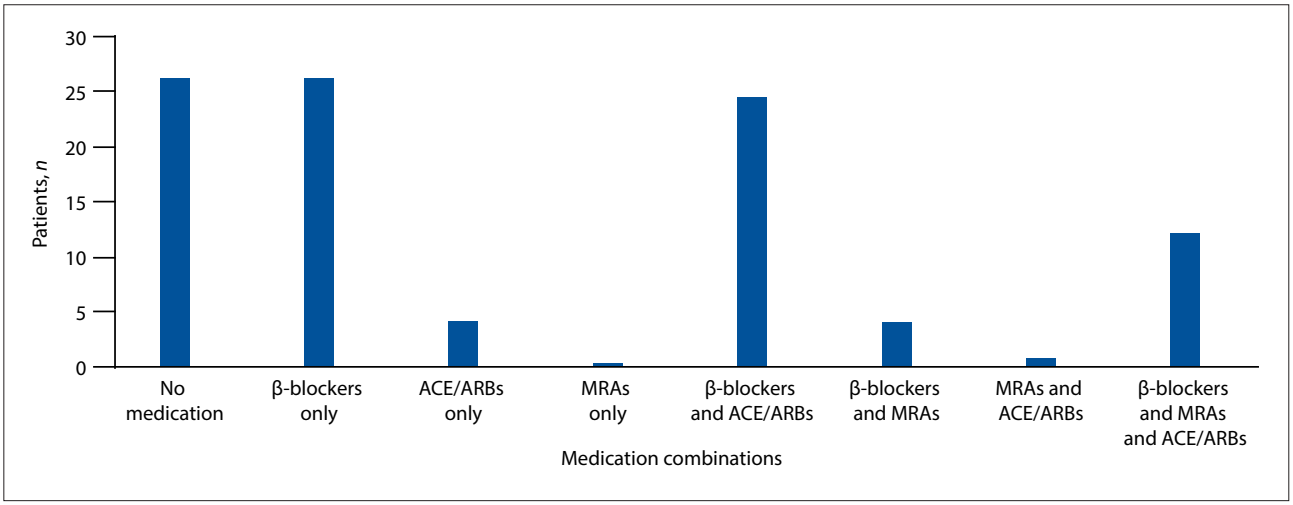

Fig. 3. Medications in patients with prosthetic mitral valves. (ACE/ARB = angiotensin coverting enzyme inhibitors/angiotensin receptor blockers; MRA = mineralocorticoid receptor antagonist.)

Table 2. Biochemical profile of patients with prosthetic mitral valve

Biochemical test	*n* (%)*	Patients with results, *n*
Hb, g/dL, median (IQR)	12.7 (11.4 - 13.7)	109
Hb category		109
Normal	75 (65.1)	
Mild anaemia	19 (17.4)	
Moderate anaemia	15 (13.8)	
Severe anaemia	4 (3.7)	
Urea, mmol/L, median (IQR)	5 (4.1 - 6.3)	110
Creatinine, mmol/L, median (IQR)	83 (69 - 94)	110
INR		180
Non-therapeutic	131 (70.4)	
Therapeutic	47 (25.3)	
None available	8 (4.3)	
Median INR, median (IQR)	2.55 (2.03 - 2.92)	180
HIV status		186
Negative	166 (89.3)	
Positive	20 (10.8)	

Hb = haemoglobin; IQR = interquartile range; INR = international normalised ratio.
*Unless otherwise indicated.

percent of patients had metallic valves, and all of these were bileaflet in nature. The median mean pressure gradient across the mitral valve was 3.5 mmHg. The median Doppler velocity index was 1.77, with an upper quartile of 2.36. These findings indicate that most patients did not exhibit any features of possible stenosis. Paravalvular regurgitation was evident in only two patients. No cases of endocarditis, structural valve deterioration, or pannus formation were found during the echocardiographic assessments. Approximately 10% of patients had a pericardial effusion, most of which were mild. Three percent of patients had a thickened pericardium.

The characteristics of patients with reduced v. preserved LVEF are compared in Table 4. Of note, patients with a reduced LVEF tended to have higher creatinine and more AF. In both univariate and multivariate analyses, the presence of AF was shown to be a strong predictor of poor LVEF, while renal function did not demonstrate a strong association.

Discussion

Our study attempts to bridge the gap in knowledge regarding outcomes of patients with mechanical MVRs in the SA setting.

The patient population was predominantly middle-aged, black African, female and overweight or obese – this underscores the expected epidemiological shift in our setting.[6] Further, a significant proportion of patients had comorbidities, such as hypertension and diabetes mellitus. These findings are similar to those of a previous study conducted in a preoperative population with mitral valve disease at Chris Hani Baragwanath Academic Hospital, Johannesburg,[15] although there was a higher incidence of comorbidities, especially hypertension (36% v. 30%) and diabetes mellitus (8% v. 4%) in our study, which may reflect changing socioeconomic and lifestyle factors. A similar, though perioperative, study investigating the perioperative outcomes of valve replacement surgeries at another centre in Johannesburg documented similar rates of comorbidities.[16] However, studies in high-income settings showed significantly higher rates of comorbid disease, with 50 - 73% of patients having hypertension and 35% with dyslipidaemia, for example.[17] This is likely explained by the fact that patients undergoing valve replacement in high-income settings are generally older, with an average age of 66 years in one study.[17]

There was a statistically significant association between female sex and isolated MVR, with 84% of all isolated MVR surgeries occurring in female patients (p=0.013). Previous studies have noted the higher incidence of mitral valve disease in female patients, which may account for this finding.[18-20] Interestingly, male patients were as likely to have isolated MVR (20 patients) v. multiple valve replacement (19 patients). Female patients were more likely to be obese, with almost all patients (94%) with a BMI >30 kg/m^2 being female (p<0.001). This association also extended to the incidence of hypertension (p=0.009) and diabetes (p=0.037). Multiple studies in the African and sub-Saharan setting have shown a higher incidence of metabolic syndrome and its associated conditions (including obesity and hypertension) among female patients of black African ethnicity.[21] Obese patients were also noted to be more likely to have had an isolated MVR (likely owing to most of them being of female sex), therefore with a higher BMI on average in this study, although the effects of obesity itself cannot be ruled out, which is a potential area for future study. More patients were HIV positive among those operated on after the year 2000, likely due to the introduction of combined ART for these patients during that time period, as well as a high incidence of HIV during that period.[22]

The available data gave the impression that the majority of valve replacements took place post 2000. We cannot conclude whether this finding is a result of patients lost to follow-up, death, or simply fewer patients operated on prior to 2000. It may be due to increasing incidence of chronic RHD and related complications, improved screening techniques for RHD, or improved access to medical and cardiology services in the last two decades; however, a lack of data makes it difficult to draw a reliable conclusion. Previous studies have shown an increasing prevalence of RHD (and sadly increasing mortality), which may account at least partially for the greater numbers of valve replacements in recent years.[23,24]

Most patients had subtherapeutic INRs and tended towards the lower end of the recommended range for patients with mechanical mitral valves. This is probably multifactorial, involving inadequate monitoring and adjustment of warfarin dosage, lack of adequate education regarding long-term vitamin K antagonist therapy (patients are given information leaflets, but these are only available in English) and socioeconomic factors.[23] This finding is consistent

Table 3. Echocardiographic characteristics of patients with prosthetic mitral valve (*N*=186)

Variable	Median (IQR)*
Left ventricle	
LVEDD, mm	46.6 (42.0 - 52.2)
LVESD, mm	34.0 (29.0 - 40.0)
IVSD, mm	5.40 (4.21 - 8.0)
LVPWD, mm	8.28 (7.0 - 11.0)
LV mass index, g/m^2	33.4 (26.2 - 44.7)
Relative wall thickness	0.37 (0.3 - 0.47)
Ejection fraction, *n* (%)	
<40	87 (46.8)
40 - 49	29 (15.6)
≥50	70 (37.6)
Left atrium	
Length, mm	54.45 (47.0 - 62.0)
Volume, mL	148.5 (101.0 - 213.0)
Indexed volume, mL/m^2	44.4 (31.3 - 67.1)
Mitral annulus, mm	42.0 (38.0 - 47.0)
Right ventricle	
RV base, mm	42.0 (39.0 - 47.0)
TAPSE, mm	16.0 (14.0 - 20.0)
RV S', cm/s	8.7 (7.5 - 10.1)
TR, m/s	2.35 (1.5 - 2.83)
RVSP, mmHg	22.0 (9.0 - 32.0)
PASP, mmHg	28.5 (17.0 - 41.0)
MPA, mm	26.0 (21.0 - 29.0)
Right atrium	
Length, mm	51.5 (4.3 - 60.0)
Tricuspid annulus, mm	38.0 (35.0 - 43.0)
Tricuspid annuloplasty ring, *n* (%)	12.0 (6.0)
Mitral valve	
Type (metallic/bioprosthetic), *n* (%)	
Bio	10.0 (5.4)
Metallic	176.0 (94.6)
Metallic type (tilting/bileaflet), *n* (%)	
Bileaflet	176.0 (100)
Tilting	0 (0)
Mean gradient, mmHg	3.5 (3.0 - 4.9)
E wave, ccm/s	158 (130.5 - 180)
A wave, ccm/s	84 (64.8 - 103)
E/A ratio	1.7 (1.2 - 2.1)
PHT, ms	112.5 (84 - 148)
DVI	1.77 (1.36 - 2.36)
EOA, cm^2	1.26 (0.93 - 1.69)
Regurgitation, *n* (%)	
Absent	184 (98.9)
Present	2 (1.1)
Tissue Doppler measurements	
Mitral E' lateral, ccm/s	8.68 (7.02 - 10.5)
Mitral E' medial, ccm/s	6.53 (5.6 - 8.19)
E/E' lateral ratio	17.4 (13.6 - 21.7)
E/E' medial ratio	22.6 (16.4 - 28.8)
Mitral S' lateral, ccm/s	6.25 (5.5 - 7.35)
Mitral S' medial, ccm/s	5.53 (4.69 - 6.43)
Pericardial findings, *n* (%)	
Effusion	
Mild (<10 mm)	19 (10.2)
Moderate (10 - 20 mm)	3 (1.6)
Severe (>20 mm)	0 (0.0)
Thickening (present)	6 (3.2)

LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; IVSD = interventricular septal diameter; LVPWD = left ventricular posterior wall diameter; LV = left ventricle; RV = right ventricle; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; RVSP = right ventricular systolic pressure; PASP = pulmonary artery systolic pressure; MPA = main pulmonary artery; E/A = E-wave A-wave ratio; PHT = pressure half-time; DVI = Doppler velocity index; EOA = effective orifice area.
*Unless otherwise indicated.

with numerous other studies in SA and other low- to middle-income countries,[25-27] but at odds with the findings at another academic hospital in Johannesburg.[28] Many patients (24 in this study) had had a CVA of undefined aetiology, and some had also had re-do surgery with an undocumented indication. It is reasonable to assume some contribution from chronically subtherapeutic INRs, as this commonly contributes to re-operation in the SA setting,[29] and CVAs in patients with prosthetic valves are often attributable to embolic disease.

Nearly 40% of patients were still in AF years after their MVR. None of the participants had evidence of patient-prosthesis mismatch or prosthetic valve stenosis, ruling out these potential reasons for the persistence of AF. The high incidence of AF may reflect a delay in time to surgery, with further progression of disease and consequent atrial remodelling, or may be indicative of late detection of disease and index presentation in a more advanced stage. Also, only four patients had maze procedures done during their valve replacement, which may explain the high incidence of persistent AF in these patients. It has previously been shown that the performance of a maze procedure in patients being operated on for valvular RHD reduces the incidence of both AF and thromboembolic complications postoperatively.[30]

A minority of patients (*n*=12; 6%) had tricuspid annuloplasty evident during their assessment. This is somewhat surprising given the frequency of tricuspid annular dilatation noted (median (IQR) tricuspid annular diameter of 38 (35 - 43) mm, and 40% >40 mm). Current guidelines suggest repairing the annulus in the presence of even mild to moderate secondary tricuspid regurgitation (TR), should the annulus measure ≥40 mm, or in the presence of features of right HF.[31] The benefits of such repair are evident, improving reverse remodelling of the right ventricle and functional status without much associated risk.[31] This is important as the risk of reoperation for TR after left-sided surgery is particularly aggravated by the entity of restriction-dilatation syndrome, originally described by Barlow.[32] The restriction-dilatation syndrome refers to worsening RV systolic function, from TR, causing diastolic shifting of the interventricular septum into the left ventricle (LV), thereby increasing LV filling pressures and further worsening the TR – this is aggravated by the presence of adhesions from previous left thoracotomy.[33]

Approximately half (47%) of all patients had biventricular dysfunction. This likely reflects the previous disease process and possible delay in presentation or definitive treatment, i.e. residual biventricular dysfunction. Other factors that may explain or contribute include comorbidities, such as HIV, obesity, hypertension, ischaemic heart disease and diabetes mellitus. The presence of AF was strongly associated with poor LV function. This may be explained in two ways: firstly, it may lend further credence to the possibility of a delay in presentation and treatment, thereby worsening both atrial and ventricular remodelling; another possibility is AF directly worsening LV function or preventing reverse remodelling (tachyarrhythmia-induced HF). A study by Suri *et al.*[34] lends credence to this hypothesis, showing a greater drop in postoperative EF in patients with AF undergoing mitral valve surgery. Many patients also had significant LV diastolic dysfunction with elevated filling pressures, which is likely due to previous disease processes, delay in time to treatment and possibly the presence of comorbidities such as hypertension, diabetes mellitus and obesity.

Interestingly, there were only two documented cases of prosthetic valve endocarditis. This is far fewer than in another study conducted at a hospital in Cape Town, SA.[35] There are two possible reasons for this: (*i*) prosthetic valve endocarditis carries a high mortality, therefore survivorship bias may play a role; and (*ii*) the relative lack of robust documentation and/or the absence of an electronic health record result in a loss of the relevant data.

Table 4. Characteristics of patients with LVEF <40% compared with patients with LVEF >40%

Variable	EF <40% (*n*=87)	EF ≥40% (*n*=99)	Univariable PRR (95% CI)	*p*-value*	Multivariable PRR (95% CI)	*p*-value
Age, median (IQR)	53 (43 - 60)	50 (38 - 61)	1.007 (0.99 - 1.02)	0.280	0.999 (0.98 - 1.02)	0.900
Male sex, *n* (%)	15 (17.2)	26 (26.3)	0.72 (0.46 - 1.13)	0.159	0.74 (0.45 - 1.22)	0.236
BMI, median (IQR)	27.1 (24.0 - 31.2)	25.5 (23.1 - 30.0)	1.01 (0.99 - 1.04)	0.314	-	-
Multiple valve replacements, *n* (%)	29 (33.3)	35 (35.3)	0.95 (0.69 - 1.32)	0.744	-	-
AF/flutter, *n* (%)	46 (52.9)	26 (26.3)	1.77 (1.31 - 2.40)	<0.001	1.77 (1.16 - 2.69)	<0.001
Anaemia, *n* (%)	10 (11.5)	13 (13.1)	0.92 (0.56 - 1.51)	0.742	-	-
Creatinine, µmol/L, median (IQR)	88.5 (73 - 98.5)	78 (58 - 92)	1.00 (0.998 - 1.02)	0.171	1.00 (0.998 - 1.011)	0.183
INR therapeutic, median (IQR)	2.56 (2.05 - 2.92)	2.55 (2.03 - 2.9)	1.06 (0.94 - 1.20)	0.370	-	-

LVEF = left ventricular ejection fraction; EF = ejection fraction; PRR = prevalence rate ratio; CI = confidence interval; IQR = interquartile range; BMI = body mass index; AF = atrial fibrillation; INR = international normalised ratio.
*Variables with $p<0.2$ were included in multivariable analysis, as well as age and sex.

Overall, our study suggests that it would be beneficial to perform MVR sooner, that maze procedures should be considered more often in patients with concomitant AF and that tricuspid annuloplasty must be offered to all patients undergoing MVR, as per standard guideline recommendations, to prevent late tricuspid regurgitation.[11] Consideration of bioprosthetic valve replacement as per guideline indications will help relieve the burden of complications related to the use of warfarin. Continued education of the public regarding RHD and related complications will result in earlier presentation and better long-term postoperative outcomes. Education regarding long-term vitamin K antagonist therapy (for both clinicians and patients) and stricter monitoring of INR should also be considered. Future studies could focus on the impact of such potential interventions, and examine the ever-changing demographic profile of our patient population. An emphasis should also be placed on the initiation and titration of guideline-directed medical therapy for HF, especially given the significant discrepancy between the number of patients with reduced EFs (almost half of the cohort) and the number of patients on at least three medications (only 12% in this study).

The strengths of this study include the significant numbers recruited, the prospective nature of data collection and the wide array of parameters examined, particularly when compared with similar studies in our setting. Weaknesses include once-off data collection, missing information in patient files and a lack of pre- and postoperative data (such as LVEF, tricuspid annular measurements and the rate of AF), including the number of MVR operations performed over time.

Conclusion

Contemporary patients with MVR were obese, middle-aged, black African females with associated comorbidities, such as hypertension and diabetes mellitus. A significant portion of patients had residual biventricular dysfunction, which was strongly correlated with the presence of AF. The most common complications were AF, HF and inadequate warfarinisation, followed by valve-specific complications. The majority of patients with HF were not on optimal guideline-directed medical therapy. These findings underline the need for more ready access to timely valve replacement, improved management of anticoagulation therapy and optimisation of guideline-directed medical therapy for HF in these patients.

Data availability. The authors will share raw data upon reasonable request from readers.

Declaration. None.

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